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## **A selfish genetic element linked to increased lifespan impacts metabolism in female house mice**

Lopes, Patricia C ; Lindholm, Anna K

**Abstract:** Gene drive systems can lead to the evolution of traits that further enhance the transmission of the driving element. In gene drive, one allele is transmitted to offspring at a higher frequency than the homologous allele. This has a range of consequences, which generally include a reduction in fitness of the carrier of the driving allele, making such systems “selfish”. The t haplotype is one such driver, found in house mice. It is linked to a reduction in litter size in matings among heterozygous animals, but also to increased lifespan in wild females that carry it. Here, we tested whether carrying the t haplotype was associated with altered resting metabolic rate (RMR). We show that females carrying the t haplotype decrease RMR as they increase in size, compared to wildtype females or males of either genotype. Our study elucidates a plausible mechanism by which a selfish genetic element increases lifespan.

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## SHORT COMMUNICATION

# A selfish genetic element linked to increased lifespan impacts metabolism in female house mice

Patricia C. Lopes<sup>1,\*</sup> and Anna K. Lindholm<sup>2</sup>

## ABSTRACT

Gene drive systems can lead to the evolution of traits that further enhance the transmission of the driving element. In gene drive, one allele is transmitted to offspring at a higher frequency than the homologous allele. This has a range of consequences, which generally include a reduction in fitness of the carrier of the driving allele, making such systems 'selfish'. The *t* haplotype is one such driver, found in house mice. It is linked to a reduction in litter size in matings among heterozygous animals, but also to increased lifespan in wild females that carry it. Here, we tested whether carrying the *t* haplotype was associated with altered resting metabolic rate (RMR). We show that females carrying the *t* haplotype decrease RMR as they increase in size, compared with wild-type females or males of either genotype. Our study elucidates a plausible mechanism by which a selfish genetic element increases lifespan.

**KEY WORDS:** Metabolic rate, Meiotic drive, Lifespan, *t* haplotype

## INTRODUCTION

Gene drive systems, or selfish genetic elements, bias inheritance to the next generation in their favour. In meiotic drivers, this is achieved by biasing which chromosome of a homologous pair is found in viable gametes. This creates intragenomic conflict over transmission, and selection on genes unlinked to the driver to eliminate the transmission bias. The evolution of resistance to drive in turn selects for better performance of the driver, which can lead to the evolution of complex adaptations of the driver to improve transmission, such as the formation of 'supergenes' that bind transmission-enhancing elements together (Schwander et al., 2014), and changes in carrier behaviour (De Crespigny et al., 2006; Runge and Lindholm, 2018) and physiology (Meade et al., 2018).

The *t* haplotype gene drive system of the house mouse (*Mus musculus*) consists of a set of overlapping inversions that suppress recombination, thereby binding hundreds of genes on an autosome together (Kelemen and Vicoso, 2018). This supergene includes genes that act post-meiotically to harm sperm that do not carry a copy of the *t*, leading to inheritance of the *t* by about 90% of a male carrier's offspring (Silver, 1985; Lindholm et al., 2013). Recombination suppression has led to the accumulation of mutations such as recessive lethal alleles, resulting in a reduction in offspring number in carriers by nearly half when mating with other carriers (Lindholm

et al., 2013; Sutter and Lindholm, 2015). Thus, the fitness of both sexes is affected, but males have an additional fitness disadvantage as they are very poor sperm competitors (Manser et al., 2017; Sutter and Lindholm, 2015). While discriminatory female mate choice against male heterozygotes would probably reduce female fitness costs (Manser et al., 2014; Sutter and Lindholm, 2015), experimental studies using mating trials have found no evidence for female mating bias (Manser et al., 2014; Sutter and Lindholm, 2016b), leading to the conclusion that females do not avoid these costs. However, in a longitudinal study of a wild house mouse population, females carrying the *t* haplotype were found to have increased lifespan (Manser et al., 2011), which would extend their reproductive lifespan, allowing the production of additional litters (Ferrari et al., 2019), but males were not differentially affected. The proximate mechanism for the increase in lifespan in *t*-carrying females is unknown. As intraspecific differences in lifespan in wild animals have been found to be associated with resting metabolic rate (RMR) in a variety of taxa [for instance, squirrels (Larivée et al., 2010), fish (Auer et al., 2018), bryozoans (Pettersen et al., 2016) and beetles (Krams et al., 2013)], we here tested whether carrying the *t* haplotype is associated with altered RMR in female mice.

## MATERIALS AND METHODS

### Animals

The mice used in the current study were laboratory-born F1 to F3 descendants of wild house mice (*Mus musculus domesticus* Schwarz and Schwarz 1943) captured from an intensively monitored study population near Illnau, Switzerland (König and Lindholm, 2012). The study population is the same in which longevity was studied (Manser et al., 2011). However, new breeding animals from the study population have been regularly added to prevent inbreeding. All tests were carried out in an animal facility at the University of Zürich, where mice were bred and kept under standardized laboratory conditions at a temperature of 22±3°C with a relative humidity of 50–60% and on a 14 h:10 h light:dark cycle with a 1 h dusk and a 1 h dawn red light phase at the beginning and end of the light phase (white light started at 06:30 h CET). The cages contained standard bedding material (Lignocel Hygienic Animal Bedding, JRS, Rosenberg, Germany), shredded paper towel and empty toilet paper rolls. Animals were provided with food (laboratory animal diet for mice, Provimi Kliba SA, Kaiseraugst, Switzerland) and water *ad libitum*. Male and female siblings were separated after weaning at 23 days of age and housed in single-sex littermate groups of 2–6 animals in standard Makrolon Type III cages. From these cages of sexually inexperienced mice, we used 15 brother pairs and 17 sister pairs for our tests (mean±s.e.m. age 67±2.1 days).

### Ethics

Animal use and experimental design were approved by the Veterinary Office Zürich, Switzerland (Kantonales Veterinäramt

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Zürich, no. 226/15). At the end of the experiment, animals were killed by CO<sub>2</sub> inhalation.

### *t* haplotype genotyping

Presence of the *t* haplotype was determined by PCR amplification of *Hba-ps4* (Lindholm et al., 2013; Schimenti and Hammer, 1990), from DNA isolated from ear punches, identifying *t* carriers (+/*t*) or homozygous wild-type (+/+) animals [homozygous (*t/t*) individuals die as embryos; Lindholm et al., 2013; Schimenti and Hammer, 1990]. The sibling pairs used for our tests contained one animal from each genotype.

### RMR measurements

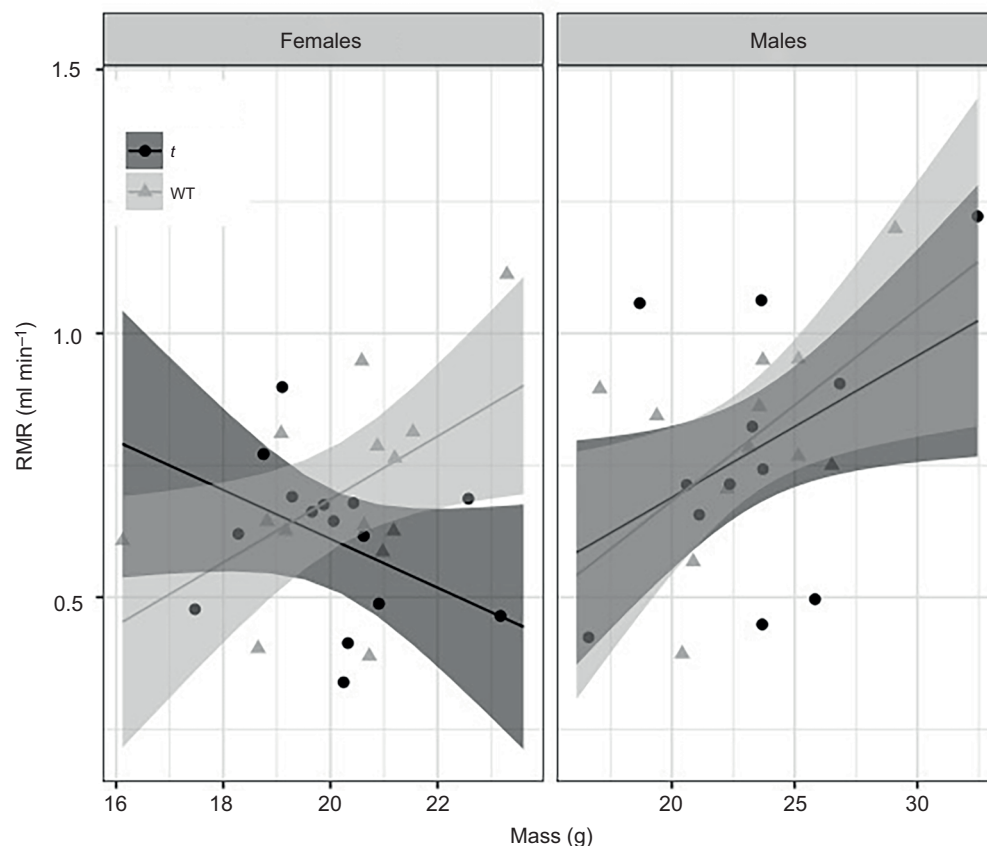
Measurement of oxygen consumption and carbon dioxide production was carried out in an eight-channel open-flow respirometry system using incurrent flow measurement. Air circulated through the chambers at a speed of 500–530 ml min<sup>-1</sup> and Drierite and Ascarite were used to remove water and CO<sub>2</sub>, respectively, from the excurrent air. A FOX O<sub>2</sub>/FOX CO<sub>2</sub> analyser (Sable Systems International, Las Vegas, NV, USA) was used to quantify the oxygen and carbon dioxide production and the software ExpeData v.1.01 (Sable Systems International) was used for recording these data. Food was removed from the cages for at least 2 h prior to mice being transferred to plastic respiration chambers (volume 2128.88 ml) and animals were kept without food and water during measurements. Eight chambers were placed inside incubators (Exo Terra) set at 30°C (within the thermal neutral zone for mice; Fischer et al., 2018); a maximum of seven contained mice, with the eighth being used as a control. The measurements started 3–4 h after lights on, which is part of the natural resting period of house mice. The rate of oxygen consumption ( $\dot{V}_{O_2}$  in ml min<sup>-1</sup>) in each chamber was measured

sequentially for 5 min each time and quantified 3–8 times in total (maximum time in the chambers was about 2 h). We quantified mouse body mass (Sartorius scale, BL1500S) before and after respirometry measurements and used the average of these two measurements in our analysis.  $\dot{V}_{O_2}$  was calculated according to Lighton (2008). The mean and standard deviation of  $\dot{V}_{O_2}$  were calculated during all possible 60 s intervals. We took RMR for each mouse as the mean oxygen consumption during the 60 s interval with lowest consumption obtained during our measurements, where standard deviation stayed within 0.015 ml min<sup>-1</sup>. As the typical standard deviation of  $\dot{V}_{O_2}$  for the chamber used as a control (containing no mice) was ~0.005 ml min<sup>-1</sup>, this procedure filtered out fluctuations of consumed oxygen that exceeded this value by threefold. Two animals (1 male and 1 female) were never in a resting state according to these parameters, so these animals and their siblings were removed from analysis.

### Statistical analysis

All tests were carried out in R version 3.3.2 (<http://www.R-project.org/>), with additional package nlme (<https://CRAN.R-project.org/package=nlme>).

We used general linear mixed models to explore the effects of sex and genotype and their interaction on RMR. The covariate body mass and its interaction with the fixed terms was also included in the model. We included a random effect of sibling pair. Fulfilment of model assumptions was inspected visually (Fig. S1). Likelihood ratio tests were used to evaluate the significance of the omitted terms. Using the nlme package, we also obtained the confidence intervals for the estimates of each term in our final model. We used paired *t*-tests to assess whether haplotype led to differences in body mass between sibling pairs within each sex.



**Fig. 1. Resting metabolic rate (RMR) as a function of body mass for wild-type (WT) and *t* haplotype carriers.** Left: females; right: males. Model estimates and 95% confidence intervals of the mean obtained from the best-fit linear mixed model are shown; points represent the raw data.

**Table 1. Genes that are upregulated or downregulated in female *t* carriers relative to wild-type and that encode proteins with metabolic functions**

Gene	Regulation in <i>t</i> carriers	log <sub>2</sub> Fold-change	FDR	Metabolic function
<i>Fmo2</i>	↑	0.76	<0.001	Potential regulator of energy homeostasis (Veeravalli et al., 2014); associated with increased lifespan in some taxa (Rossner et al., 2017)
<i>Adrb3</i>	↑	0.92	0.0330	Involved in the regulation of lipolysis and thermogenesis (P25962)
<i>Rdh16</i>	↑	0.44	0.0166	Oxidoreductase capable of oxidizing retinols and steroids (O54909)
<i>Acot4</i>	↑	0.43	0.0379	Acyl-CoA thioesterase involved in fatty acid metabolism (Q8BWN8)
<i>Acot3</i>	↑	0.98	<0.001	Acyl-CoA thioesterase involved in fatty acid metabolism (Q9QYR7)
<i>Cyp2d40</i>	↑	0.50	0.0709	In humans, many of the genes in the cytochrome P450 (CYP) family code for enzymes involved in eicosanoid metabolism (Nebert et al., 2013)
<i>H2-Ke6</i>	↑	0.51	0.0673	Dehydrogenase that catalyses conversion of oestradiol to oestrone and plays a role in fatty acid metabolism (P50171)
<i>Igfbp2</i>	↓	-0.71	0.0011	Capable of regulating glucose metabolism (Hedbacker et al., 2010)

↑, upregulation; ↓, downregulation; FDR, false discovery rate. Where the protein encoded by the gene had been manually annotated and reviewed in the UniProt database (The UniProt Consortium, 2019), we provide their accession number in the table as a reference for functions. Otherwise, we provide primary literature references.

## RESULTS AND DISCUSSION

We found a significant interaction of body mass, sex and genotype ( $\chi^2=11.63$ , d.f.=1,  $P<0.001$ , Fig. 1; Table S1 displays the coefficient estimates for all fixed terms in the final model). In males, RMR increased with body mass, whereas in females, this relationship was strongly affected by genotype (Fig. 1). Wild-type females increased RMR as body mass increased, while *t*-carrying females decreased RMR with increasing body mass. Within sibling pairs, body mass did not differ between *t*-carriers and wild-types (paired *t*-test: females  $t_{15}=0.64$ ,  $P=0.53$ ; males  $t_{13}=-0.199$ ,  $P=0.85$ ).

Previous work found that, in female house mice, the presence of a selfish genetic element, the *t* haplotype, was linked to increased lifespan (Manser et al., 2011). Although the directionality of the relationship between RMR and lifespan is inconsistent in the literature, a relationship between reduced RMR and lifespan has been established in some species (Auer et al., 2018; Krams et al., 2013; Larivée et al., 2010; Pettersen et al., 2016), including mice (Duarte and Speakman, 2014; Książek et al., 2004). These findings led us to hypothesize that the *t* haplotype may impose a reduction in RMR in females. Indeed, we found that as body mass increased, female, but not male, carriers had a lower RMR than non-carriers. Differences in metabolic rate may arise through differences in body composition, such as fatness (Duarte and Speakman, 2014) or organ size (Książek et al., 2004), or in tissue-specific metabolism (Speakman, 2013). However, as the females were sexually inexperienced, possible effects of gestation or lactation can be excluded. What mechanism could result in the reduction in RMR in *t* females but not *t* males?

To provide possible explanations for this pattern, we explored a publicly available RNA-seq dataset from an independent experiment in house mice in which gene expression was compared between *t*-carrier and wild-type siblings in brain, reproductive organs and liver (Lindholm et al., 2019). Importantly, the mice used were derived from the same population as those in the current study. As an organ critical for metabolism, we focused on the liver and investigated genes that showed differential expression in *t* carriers compared with wild-type in females but not in males. We found that a number of genes involved in lipolysis, fatty acid and steroid oxidation and hydrolysis (*Fmo2*, *Adrb3*, *Rdh16*, *Acot4*, *Acot3*, *Cyp2d40*, *H2-Ke6*) were upregulated and one gene involved in hepatic glucose production (*Igfbp2*) was downregulated in *t* carriers relative to wild-type females (Table 1) but there was no difference in *t* carriers relative to wild-type males. The differences in the pattern of expression of these genes suggest that, relative to wild-type,

*t*-carrying females may use certain metabolic pathways (such as lipid oxidation) more readily than others (such as glycolysis), which can ultimately impact their energy homeostasis and RMR. Exactly how the RMR difference between female *t* carriers and non-carriers arises needs to be determined to better understand the complex associations between energetics and behaviour, as well as the complex evolution of the *t* haplotype.

A reduced RMR correlated with increased lifespan in females could be an adaptation to compensate for the main fitness disadvantage to females associated with the *t* haplotype: strongly reduced litter sizes when mating with male carriers (Lindholm et al., 2013; Manser et al., 2014; Sutter and Lindholm, 2015). Living longer, to allow the production of additional litters (Ferrari et al., 2019), would be advantageous to the carrier, and increase transmission of the *t* haplotype. Why would wild-type females not adopt this same strategy? It has been proposed that a link between RMR and fitness may depend on the quality of the environment (Burton et al., 2011). This ‘context-dependence’ hypothesis predicts that low-RMR individuals will only have relatively high fitness when conditions are poor, but that under favourable conditions, their fitness will be lower than that of high-RMR individuals. Populations living in fluctuating and/or unpredictable environments may allow for the coexistence of the two strategies. Male carriers, however, have additional strong fitness costs from another source, reduced sperm competitive ability (Manser et al., 2017; Sutter and Lindholm, 2015), and would benefit the most from mate-guarding to avoid sperm competition (Sutter and Lindholm, 2016a). In males, reduced RMR potentially interferes with the ability to defend territories (Réale et al., 2010) and this may have selected for sex-specific effects. This system is therefore interesting for further exploration of intraspecific life-history variation.

It is still puzzling how the *t* haplotype can persist in wild populations, given the fitness disadvantages to its carriers. One compensatory mechanism, as suggested in this study, could be through decreases in the RMR of female carriers, increasing the probability of survival to the next reproductive event.

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## Competing interests

The authors declare no competing or financial interests.



**Author contributions**

Conceptualization: P.C.L., A.K.L.; Methodology: A.K.L.; Formal analysis: P.C.L.; Investigation: P.C.L.; Writing - original draft: P.C.L., A.K.L.; Writing - review & editing: P.C.L., A.K.L.; Funding acquisition: A.K.L.

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**Data availability**

Data are available from the Dryad digital repository (Lopes and Lindholm, 2019): 10.5061/dryad.k71rd89.

**Supplementary information**

Supplementary information available online at <http://jeb.biologists.org/lookup/doi/10.1242/jeb.212704.supplemental>

**References**

- Auer, S. K., Dick, C. A., Metcalfe, N. B. and Reznick, D. N. (2018). Metabolic rate evolves rapidly and in parallel with the pace of life history. *Nat. Commun.* **9**, 14. doi:10.1038/s41467-017-02514-z
- Burton, T., Killen, S. S., Armstrong, J. D. and Metcalfe, N. B. (2011). What causes intraspecific variation in resting metabolic rate and what are its ecological consequences? *Proc. R. Soc. B* **278**, 3465-3473. doi:10.1098/rspb.2011.1778
- De Crespigny, F. E. C., Pitt, T. D. and Wedell, N. (2006). Increased male mating rate in *Drosophila* is associated with Wolbachia infection. *J. Evol. Biol.* **19**, 1964-1972. doi:10.1111/j.1420-9101.2006.01143.x
- Duarte, L. C. and Speakman, J. R. (2014). Low resting metabolic rate is associated with greater lifespan because of a confounding effect of body fatness. *Age* **36**, 9731. doi:10.1007/s11357-014-9731-3
- Ferrari, M., Lindholm, A. K. and König, B. (2019). Fitness consequences of female alternative reproductive tactics in house mice (*Mus musculus domesticus*). *Am. Nat.* **193**, 106-124. doi:10.1086/700567
- Fischer, A. W., Cannon, B. and Nedergaard, J. (2018). Optimal housing temperatures for mice to mimic the thermal environment of humans: an experimental study. *Mol. Metab.* **7**, 161-170. doi:10.1016/j.molmet.2017.10.009
- Hedbacker, K., Birsoy, K., Wysocki, R. W., Asilmaz, E., Ahima, R. S., Farooqi, I. S. and Friedman, J. M. (2010). Antidiabetic effects of IGFBP2, a leptin-regulated gene. *Cell Metab.* **11**, 11-22. doi:10.1016/j.cmet.2009.11.007
- Kelemen, R. K. and Vicoso, B. (2018). Complex history and differentiation patterns of the t-haplotype, a mouse meiotic driver. *Genetics* **208**, 365-375. doi:10.1534/genetics.117.300513
- König, B. and Lindholm, A. K. (2012). The complex social environment of female house mice (*Mus domesticus*). In *Evolution of the House Mouse* (eds. M. Macholán, S. J. E. Baird, P. Munclinger and J. Piálek), pp. 114-134. Cambridge: Cambridge University Press.
- Krams, I., Kivleniece, I., Kuusik, A., Krama, T., Mänd, R., Rantala, M. J., Znotiņa, S., Freeberg, T. M. and Mänd, M. (2013). Predation promotes survival of beetles with lower resting metabolic rates. *Entomol. Exp. Appl.* **148**, 94-103. doi:10.1111/eea.12079
- Książek, A., Konarzewski, M. and Łapo, I. B. (2004). Anatomic and energetic correlates of divergent selection for basal metabolic rate in laboratory mice. *Physiol. Biochem. Zool.* **77**, 890-899. doi:10.1086/425190
- Larivée, M. L., Boutin, S., Speakman, J. R., McAdam, A. G. and Humphries, M. M. (2010). Associations between over-winter survival and resting metabolic rate in juvenile North American red squirrels. *Funct. Ecol.* **24**, 597-607. doi:10.1111/j.1365-2435.2009.01680.x
- Lighton, J. R. B. (2008). *Measuring Metabolic Rates: A Manual for Scientists*. Oxford, Oxford University Press.
- Lindholm, A. K., Musolf, K., Weidt, A. and König, B. (2013). Mate choice for genetic compatibility in the house mouse. *Ecol. Evol.* **3**, 1231-1247. doi:10.1002/ece3.534
- Lindholm, A., Sutter, A., Künzel, S., Tautz, D. and Rehrauer, H. (2019). Effects of a male meiotic driver on male and female transcriptomes in the house mouse. *Proc. R. Soc. B* **286**, 20191927. doi:10.1098/rspb.2019.1927
- Lopes, P. C. and Lindholm, A. K. (2019). Data from: A selfish genetic element linked to increased lifespan impacts metabolism in female house mice. *Dryad Digital Repository*. <https://doi.org/10.5061/dryad.k71rd89>
- Manser, A., Lindholm, A. K., König, B. and Bagheri, H. C. (2011). Polyandry and the decrease of a selfish genetic element in a wild house mouse population. *Evolution* **65**, 2435-2447. doi:10.1111/j.1558-5646.2011.01336.x
- Manser, A., König, B. and Lindholm, A. K. (2014). Female house mice avoid fertilization by t haplotype incompatible males in a mate choice experiment. *J. Evol. Biol.* **28**, 54-64. doi:10.1111/jeb.12525
- Manser, A., Lindholm, A. K., Simmons, L. W. and Firman, R. C. (2017). Sperm competition suppresses gene drive among experimentally evolving populations of house mice. *Mol. Ecol.* **26**, 5784-5792. doi:10.1111/mec.14215
- Meade, L. C., Dinneen, D., Kad, R., Lynch, D. M., Fowler, K. and Pomiankowski, A. (2018). Ejaculate sperm number compensation in stalk-eyed flies carrying a selfish meiotic drive element. *Heredity* **122**, 916-926. doi:10.1038/s41437-018-0166-y
- Nebert, D. W., Wikvall, K. and Miller, W. L. (2013). Human cytochromes P450 in health and disease. *Philos. Trans. R. Soc. B Biol. Sci.* **368**, 20120431. doi:10.1098/rstb.2012.0431
- Pettersen, A. K., White, C. R. and Marshall, D. J. (2016). Metabolic rate covaries with fitness and the pace of the life history in the field. *Proc. R. Soc. B* **283**, 20160323. doi:10.1098/rspb.2016.0323
- Réale, D., Garant, D., Humphries, M. M., Bergeron, P., Careau, V. and Montiglio, P.-O. (2010). Personality and the emergence of the pace-of-life syndrome concept at the population level. *Philos. Trans. R. Soc. B Biol. Sci.* **365**, 4051-4063. doi:10.1098/rstb.2010.0208
- Rosner, R., Kaeberlein, M. and Leiser, S. F. (2017). Flavin-containing monooxygenases in aging and disease: emerging roles for ancient enzymes. *J. Biol. Chem.* **292**, 11138-11146. doi:10.1074/jbc.R117.779678
- Runge, J.-N. and Lindholm, A. K. (2018). Carrying a selfish genetic element predicts increased migration propensity in free-living wild house mice. *Proc. R. Soc. B* **285**, 20181333. doi:10.1098/rspb.2018.1333
- Schimenti, J. and Hammer, M. (1990). Rapid identification of mouse t haplotypes by PCR polymorphism (PCR). *Mouse Genome* **87**, 108.
- Schwander, T., Libbrecht, R. and Keller, L. (2014). Supergenes and complex phenotypes. *Curr. Biol.* **24**, R288-R294. doi:10.1016/j.cub.2014.01.056
- Silver, L. M. (1985). Mouse tau haplotypes. *Ann. Rev. Genet.* **19**, 179-208. doi:10.1146/annurev.ge.19.120185.001143
- Speakman, J. R. (2013). Measuring energy metabolism in the mouse – theoretical, practical, and analytical considerations. *Front. Physiol.* **4**, 34. doi:10.3389/fphys.2013.00034
- Sutter, A. and Lindholm, A. K. (2015). Detrimental effects of an autosomal selfish genetic element on sperm competitiveness in house mice. *Proc. R. Soc. B* **282**, 20150974. doi:10.1098/rspb.2015.0974
- Sutter, A. and Lindholm, A. K. (2016a). Meiotic drive changes sperm precedence patterns in house mice: potential for male alternative mating tactics? *BMC Evol. Biol.* **16**, 133. doi:10.1186/s12862-016-0710-4
- Sutter, A. and Lindholm, A. K. (2016b). No evidence for female discrimination against male house mice carrying a selfish genetic element. *Curr. Zool.* **62**, 675-685. doi:10.1093/cz/zow063
- The UniProt Consortium (2019). UniProt: a worldwide hub of protein knowledge. *Nucleic Acids Res.* **47**, D506-D515. doi:10.1093/nar/gky1049
- Veeravalli, S., Omar, B. A., Houseman, L., Hancock, M., Gonzalez Malagon, S. G., Scott, F., Janmohamed, A., Phillips, I. R. and Shephard, E. A. (2014). The phenotype of a flavin-containing monooxygenase knockout mouse implicates the drug-metabolizing enzyme FMO1 as a novel regulator of energy balance. *Biochem. Pharmacol.* **90**, 88-95. doi:10.1016/j.bcp.2014.04.007